



## RYR2 gene

ryanodine receptor 2

### Normal Function

The *RYR2* gene provides instructions for making a protein called ryanodine receptor 2. This protein is part of a family of ryanodine receptors, which form channels that transport positively charged calcium atoms (calcium ions) within cells.

Channels made with the ryanodine receptor 2 protein are found in heart (cardiac) muscle cells called myocytes. These channels are embedded in the outer membrane of a cell structure called the sarcoplasmic reticulum, which acts as a storage center for calcium ions. The RYR2 channel controls the flow of calcium ions out of the sarcoplasmic reticulum.

For the heart to beat normally, the cardiac muscle must tense (contract) and relax in a coordinated way. This cycle of muscle contraction and relaxation results from the precise control of calcium ions within myocytes. In response to certain signals, the RYR2 channel releases calcium ions from the sarcoplasmic reticulum into the surrounding cell fluid (the cytoplasm). The resulting increase in calcium ion concentration triggers the cardiac muscle to contract, which pumps blood out of the heart. Calcium ions are then transported back into the sarcoplasmic reticulum, and the cardiac muscle relaxes. In this way, the release and reuptake of calcium ions in myocytes produces a regular heart rhythm.

### Health Conditions Related to Genetic Changes

arrhythmogenic right ventricular cardiomyopathy

catecholaminergic polymorphic ventricular tachycardia

More than 70 mutations in the *RYR2* gene have been found to cause catecholaminergic polymorphic ventricular tachycardia (CPVT). Almost all of these mutations change single protein building blocks (amino acids) in the ryanodine receptor 2 protein. These mutations alter the structure and function of the RYR2 channel.

Researchers are uncertain how *RYR2* gene mutations lead to ventricular tachycardia, the abnormally fast and irregular heart rhythm (arrhythmia) that is characteristic of CPVT. Some studies have suggested that mutations interfere with the regulation of the RYR2 channel. Other studies have found that the altered RYR2 channel stays open abnormally, allowing calcium ions to "leak" out of the sarcoplasmic reticulum.

It is clear that changes in the structure and function of the RYR2 channel disrupt the careful control of calcium ion flow in myocytes, which can trigger an abnormal heart rhythm in people with CPVT.

### other disorders

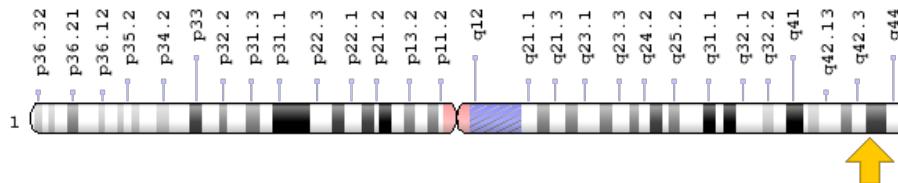
Several other mutations in the *RYR2* gene have been found to cause a heart condition called arrhythmogenic right ventricular cardiomyopathy (ARVC). This condition causes part of the heart muscle to break down over time, which increases the risk of arrhythmia and sudden death.

The *RYR2* gene mutations responsible for ARVC change single amino acids in the ryanodine receptor 2 protein. These mutations alter the structure of the RYR2 channel, which probably allows calcium ions to "leak" out of the sarcoplasmic reticulum. This failure of calcium regulation within myocytes can trigger the abnormal heart rhythm characteristic of ARVC.

### **Chromosomal Location**

Cytogenetic Location: 1q43, which is the long (q) arm of chromosome 1 at position 43

Molecular Location: base pairs 237,042,208 to 237,833,988 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

### **Other Names for This Gene**

- ARVC2
- ARVD2
- cardiac muscle ryanodine receptor
- cardiac muscle ryanodine receptor-calcium release channel
- CPVT1
- ryanodine receptor 2 (cardiac)
- VTSIP

## **Additional Information & Resources**

### Educational Resources

- Madame Curie Bioscience Database: Intracellular Ca<sup>2+</sup> Release Channels  
<https://www.ncbi.nlm.nih.gov/books/NBK5959/#A37642>

### GeneReviews

- Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy  
<https://www.ncbi.nlm.nih.gov/books/NBK1131>
- Catecholaminergic Polymorphic Ventricular Tachycardia  
<https://www.ncbi.nlm.nih.gov/books/NBK1289>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28RYR2%5BTIAB%5D%29+OR+%28ryanodine+receptor+2%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

### OMIM

- ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA, FAMILIAL, 2  
<http://omim.org/entry/600996>
- RYANODINE RECEPTOR 2  
<http://omim.org/entry/180902>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_RYR2.html](http://atlasgeneticsoncology.org/Genes/GC_RYR2.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=RYR2%5Bgene%5D>
- HGNC Gene Family: EF-hand domain containing  
<http://www.genenames.org/cgi-bin/genefamilies/set/863>
- HGNC Gene Family: Ryanodine receptors  
<http://www.genenames.org/cgi-bin/genefamilies/set/287>
- HGNC Gene Symbol Report  
[http://www.genenames.org/cgi-bin/gene\\_symbol\\_report?q=data/hgnc\\_data.php&hgnc\\_id=10484](http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10484)

- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/6262>
- UniProt  
<http://www.uniprot.org/uniprot/Q92736>

## Sources for This Summary

- Bhuiyan ZA, van den Berg MP, van Tintelen JP, Bink-Boelkens MT, Wiesfeld AC, Alders M, Postma AV, van Langen I, Mannens MM, Wilde AA. Expanding spectrum of human RYR2-related disease: new electrocardiographic, structural, and genetic features. *Circulation*. 2007 Oct 2;116(14):1569-76. Epub 2007 Sep 17.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17875969>
- Cerrone M, Napolitano C, Priori SG. Catecholaminergic polymorphic ventricular tachycardia: A paradigm to understand mechanisms of arrhythmias associated to impaired Ca(2+) regulation. *Heart Rhythm*. 2009 Nov;6(11):1652-9. doi: 10.1016/j.hrthm.2009.06.033. Epub 2009 Jun 30. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19879546>
- Györke S. Molecular basis of catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm*. 2009 Jan;6(1):123-9. doi: 10.1016/j.hrthm.2008.09.013. Epub 2008 Sep 16. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/19121813>
- Liu N, Priori SG. Disruption of calcium homeostasis and arrhythmogenesis induced by mutations in the cardiac ryanodine receptor and calsequestrin. *Cardiovasc Res*. 2008 Jan 15;77(2):293-301. Epub 2007 Aug 14. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/18006488>
- Paavola J, Viitasalo M, Laitinen-Forsblom PJ, Pasternack M, Swan H, Tikanen I, Toivonen L, Kontula K, Laine M. Mutant ryanodine receptors in catecholaminergic polymorphic ventricular tachycardia generate delayed afterdepolarizations due to increased propensity to Ca<sup>2+</sup> waves. *Eur Heart J*. 2007 May;28(9):1135-42. Epub 2007 Mar 8.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17347175>
- Postma AV, Denjoy I, Kambllock J, Alders M, Lupoglazoff JM, Vaksmann G, Dubosq-Bidot L, Sebillon P, Mannens MM, Guicheney P, Wilde AA. Catecholaminergic polymorphic ventricular tachycardia: RYR2 mutations, bradycardia, and follow up of the patients. *J Med Genet*. 2005 Nov; 42(11):863-70.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/16272262>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735955/>
- Priori SG, Napolitano C, Tiso N, Memmi M, Vignati G, Bloise R, Sorrentino V, Danieli GA. Mutations in the cardiac ryanodine receptor gene (hRyR2) underlie catecholaminergic polymorphic ventricular tachycardia. *Circulation*. 2001 Jan 16;103(2):196-200.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/11208676>
- Tiso N, Stephan DA, Nava A, Bagattin A, Devaney JM, Stanchi F, Larderet G, Brahmbhatt B, Brown K, Baucé B, Muriago M, Basso C, Thiene G, Danieli GA, Rampazzo A. Identification of mutations in the cardiac ryanodine receptor gene in families affected with arrhythmogenic right ventricular cardiomyopathy type 2 (ARVD2). *Hum Mol Genet*. 2001 Feb 1;10(3):189-94.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/11159936>

---

Reprinted from Genetics Home Reference:  
<https://ghr.nlm.nih.gov/gene/RYR2>

Reviewed: December 2009

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications  
U.S. National Library of Medicine  
National Institutes of Health  
Department of Health & Human Services